

REMARKS

Claims 76-86 are pending, and were rejected by the Examiner. Claim 76 has been amended to recite a method for decreasing clot formation that includes administering to a patient an anticoagulant and a protein C or activated protein C polypeptide, wherein the polypeptide contains the amino acid sequence of SEQ ID NO:1 with two, three, four, or five substitutions at positions selected from 10, 11, 28, 32, or 33. Claims 79 and 86 have been amended to depend from claim 76, and to include analogous language. Support for these amendments can be found throughout Applicant's specification, including, for example, at page 10, line 31 to page 11, page 20, line 27 to page 21, line 3, line 32, page 37, line 28 to page 39, line 16, page 42, line 11 to page 43, line 17, page 49, line 8 to page 50, line 5, and in Figures 12, 13, and 16. No new matter has been added.

In light of these amendments and the following remarks, Applicant respectfully requests reconsideration and allowance of claims 76-86.

Rejections under 35 U.S.C. § 112, second paragraph

The Examiner rejected claims 76-86 under 35 U.S.C. 112, second paragraph, as being indefinite. Specifically, the Examiner stated that claims 76, 79, and 86 recite an "effective amount" of protein C or activated protein C without providing what effect the protein is intended to have.

Claims 76, 79, and 86 have been amended to recite methods for decreasing clot formation. Thus, the present claims are unambiguous as to the intended effect of the anticoagulant agent and the protein C or activated protein C polypeptide. In light of these amendments, Applicant respectfully requests withdrawal of the rejection of claims 76-86 under 35 U.S.C. § 112, second paragraph.

Rejections under 35 U.S.C. § 103

The Examiner rejected claims 76, 77, and 79 under 35 U.S.C. § 103(a) as being unpatentable over Smirnov et al. (U.S. Patent No. 5,837,843). The Examiner also rejected

claims 76-86 under 35 U.S.C. 103(a) as being unpatentable over Wakako et al. (EP 0296413) in view of Grinnell et al. (U.S. Patent No. 6,071,514).

The Examiner stated that the Smirnov et al. patent teaches an activated protein C polypeptide having a modified Gla domain that contains amino acid substitutions at positions 10, 11, 28, 32, and 33 as compared to SEQ ID NO:1 of the present application. The Examiner also alleged that the Smirnov et al. patent suggests that the modified protein C described therein could be used in the treatment of conditions in which protein S is low, such as with warfarin treatment, and thus implies that the modified protein C can be used in combination with warfarin. Thus, the Examiner stated that it would have been obvious to one of ordinary skill in the art at the time the invention was made to use the modified protein C polypeptide of Smirnov et al. in combination with warfarin.

Similarly, the Examiner rejected claims 76-86 under 35 U.S.C. 103(a) as being unpatentable over Wakako et al. (EP 0296413) in view of Grinnell et al. (U.S. Patent No. 6,071,514). The Examiner stated that the Wakako et al. patent application teaches a modified protein C containing substitutions at positions 10, 11, 28, 32, and 33 with respect to SEQ ID NO:1 of the present invention, with a glycine at position 11, a glutamate at position 32, and an aspartate at position 33. The Examiner also stated that while the Wakako et al. reference does not specifically disclose a method of treatment that includes administering the modified protein C and an anticoagulant, the Grinnell et al. patent discloses a combination therapy with human activated protein C and an antiplatelet (anticoagulant) agent such as aspirin or heparin. Thus, the Examiner alleged that it would have been obvious to one of ordinary skill in the art at the time the application was filed to use the protein C polypeptide of the Wakako et al. application in combination with an anticoagulant as described in the Grinnell et al. patent.

Applicant respectfully disagrees with these rejections. As described above, claim 76 has been amended to recite a method for decreasing clot formation by administering an anticoagulant agent and a protein C or activated protein C polypeptide having a modified GLA domain that contains the amino acid sequence of SEQ ID NO:1 in which two, three, four, or five amino acid substitutions are made at positions selected from residues 10, 11, 28, 32, and 33. Smirnov et al.

does not teach or suggest a method for decreasing clot formation using a protein C or modified protein C polypeptide in which amino acids at specific positions are substituted in the Gla domain. Rather, the Smirnov et al. patent teaches use of a human protein C polypeptide in which the human protein C Gla domain has been replaced with the prothrombin Gla domain, without any suggestion of substitutions at particular residues in the protein C Gla domain, let alone those of the present invention. Without specifying the substituted positions of the present invention, Smirnov et al. does not teach or suggest all the limitations of the claims. Thus, the presently claimed methods are not obvious over Smirnov et al.

The Wakako et al. patent application teaches a human protein C polypeptide in which the Gla domain is replaced by the Gla domain of factor X. As described above, the method of amended claim 76 utilizes a protein C or activated protein C polypeptide having a modified GLA domain in which SEQ ID NO:1 has two, three, four, or five amino acid substitutions made at positions selected from residues 10, 11, 28, 32, and 33. The Wakako et al. reference does not teach or suggest methods of using such protein C polypeptides having modifications at specific residues in the Gla domain, and in particular, does not teach or suggest substitution of the residues specified in the present invention. The Grinnell et al. reference does not teach or suggest protein C polypeptides having amino acid substitutions in the Gla domain, and therefore fails to remedy the deficiencies of Wakako et al. with respect to the present invention. Accordingly, Wakako et al. in view of Grinnell et al. does not teach or suggest all of the limitations of the claims and thereby does not render the present invention obvious.

In light of the above, Applicant respectfully requests withdrawal of the rejection of claims 76-86 under 35 U.S.C. § 103(a).

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CONCLUSION

Applicant respectfully requests that claims 76-86 be allowed. Enclosed is a check for the Petition for Extension of Time fee. Please apply any other charges or credits to deposit account 06-1050. The Examiner is invited to telephone the undersigned agent if such would further prosecution.

Respectfully submitted,

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